UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,683	04/07/2006	Frieder Schwenk	100725-49 KGB	6034

27384 7590 12/30/2008

NORRIS, MCLAUGHLIN & MARCUS, PA
875 THIRD AVENUE
18TH FLOOR
NEW YORK, NY 10022

EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	

MAIL DATE	DELIVERY MODE
12/30/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,683	SCHWENK ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-19,24,25,28-41 and 43-56* is/are pending in the application.

4a) Of the above claim(s) *47 and 49-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-19,24,25,28-41,43-46,48 and 53-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-16, 20-23, 26, 27, 42 have been canceled. Claim 66 has been added Claims 17-19, 24, 25, 28-41, 43-56 are pending.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant's arguments filed 10-6-08 have been fully considered but they are not persuasive.

Election/Restrictions

Claims 47 and 49-52 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in the reply filed on 1-28-08.

Claims 17-19, 24, 25, 28-41, 43-46, 48 and 53-56 are under consideration.

Claim Rejections - 35 USC § 101

The rejection of claims 17-19, 24, 25, 28-41, 43-46, 48 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter has been withdrawn in view of the amendment.

Claims 53-55 remain and claim 56 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter has been withdrawn in view of the amendment. Claims 53-55 still encompass transgenic multi-cell organisms that are human. Claim 55 encompasses any model of animal disease including humans.

Claim 56 encompasses introducing acceptor DNA into a human eukaryotic cell. The claims should be limited to

Claim Rejections - 35 USC § 112

New Matter

Claims 31 and 53-56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The amendment to claim 31 is new matter. Support cannot be found for a promoter "heterologous relative to the Rosa26 locus" and none has been provided.

The amendment to claim 53 is new matter. Support cannot be found for expressing a gene of interest and evaluating the function of the gene and none has been provided.

The amendment to claim 54 is new matter. Support cannot be found for evaluating the effect of the drug on the gene and none has been provided.

The amendment to claim 55 is new matter. Support cannot be found for providing an animal model of disease, "expression of the gene of interest models a disease state of said animal", contacting a "biological entity" with a drug candidate, and evaluating the effect of the drug on the gene of interest, and none has been provided.

Claim 56 is new matter. Support cannot be found for the steps or structures in the acceptor DNA as claimed, and none has been provided by applicants.

Enablement

The rejection of claims 17-19, 24, 25, 28-41, 43-46, 48 and 53-55 under 35 U.S.C. 112, first paragraph, enablement has been withdrawn in view of the amendment.

Indefiniteness

Claims 17-19, 24, 25, 28-41, 43-46, 48 and 53-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection of claim 17 regarding the term "starting" has been withdrawn in view of the amendment.

The rejection of claim 18 regarding how the targeting vector relates to the "functional DNA sequence" or "gene expression cassette" in claim 17 has been withdrawn in view of the amendment.

Claims 18 and 19 as amended are clear because they further limit how the functional DNA sequence is introduced while simultaneously further limiting the structure of the functional DNA sequence.

Claim 17 is indefinite because "mammalian eukaryotic" cells are unclear. By definition, a mammalian cell is a eukaryotic cell. Using both adjectives to describe a cell is unclear. Deletion of eukaryotic throughout all of the claims is required. Limiting the phrase in all the claims to "non-human mammalian cells" will suffice.

Claim 18 remains indefinite as amended because the phrase "flanked by DNA sequences homologous to the Rosa26 locus" is unclear and does not clearly set for the structure of the homology arms or that the sequences are from a Rosa26 gene.

Flanking arms of homology in this case are from a Rosa26 gene, not the "position" or "locus" of the Rosa26 gene. Replacing "locus" with --gene-- is required.

Claim 19 remains indefinite because the phrase "site specific recombinase mediated recombination" is unclear. The metes and bounds of the phrase are not defined in the specification or the art at the time of filing. Therefore, those of skill would not know when they had performed that type of site specific recombination. Applicants argue the technique was well known in the art and cite pg 9-10. Applicants' argument is not persuasive. The art did not define when recombination was "specific" to a site or how close recombination must be to be "specific."

Claim 28 remains indefinite because the metes and bounds of what applicants consider "primary" cannot be determined. The term is not defined in the specification or the art at the time of filing. Applicants argue the term was used in the art at the time of filing. Applicants' argument is not persuasive. The specification and the art at the time of filing did not define "primary" cells. Without a definition, those of skill would not know when they were infringing on the claim.

Claim 30 remains indefinite because the phrase "pharmaceutically active proteins and peptides" is unclear. It is unclear when a protein or peptide is pharmaceutically active as claimed. Applicants argue the phrase "pharmaceutically active" was used in the art at the time of filing. Applicants' argument is not persuasive. The specification and the art at the time of filing did not define when proteins and peptides are "pharmaceutically active" as claimed. Without a definition, those of skill would not know when they were infringing on the claim.

The rejection regarding claim 31 has been withdrawn in view of the amendment.

Claim 31 is indefinite because it cannot be determined how a promoter can be heterolgous to the position or "locus" of the Rosa26 gene. Clarification is required.

The metes and bounds of what applicants consider an "inducible ubiquitous promoter" and "inducible tissue specific promoter" in claim 32 cannot be determined. The structure of such promoters is not defined in the specification or the art at the time of filing. Applicants argue the phrases are well known promoter genera and species. Applicants point to the first paragraph on pg 8. Applicants' argument is not persuasive. The specification and the art at the time of filing did not define which promoters are "inducible ubiquitous promoters" and "inducible tissue specific promoters". Without a definition, those of skill would not know when they were infringing on the claim.

The metes and bounds of what applicants consider a "CAGGS, hCMV, PGK, FABP, Lck, CamKII, CD19... ...aP2... ...MCK, MyHC, WAP, Col2A, Mx, tet and trex" promoter in claim 33 cannot be determined. The structure of such promoters is not defined in the specification or the art at the time of filing. The abbreviations should be spelled out where necessary or applicants should point to the definition of such abbreviations in the specification or the art at the time of filing. Applicants argue the phrases are well known promoter genera and species. Applicants point to the first paragraph on pg 8. Applicants' argument is not persuasive. The specification does not teach what the abbreviations stand for. Clarification is required.

Claim 34 remains indefinite because the claim has the limitation of "additional recombinase recognition sites" without requiring any recombinase recognition sites to begin with.

Claim 35 is indefinite because the phrase "the targeting vector and recombination vector" lacks antecedent basis in claims 18 and 19. The phrase "the targeting vector" lacks antecedent basis in claim 19 and the phrase "the recombination vector" lacks antecedent basis in claim 18.

The rejection of claim 36 regarding the phrase "the DNA sequences homologous to the Rosa26 locus" has been withdrawn in view of the amendment.

Claim 38 remains indefinite because it does not clearly set forth the cells are mouse cells. The phrase "wherein the eukaryotic cells are mouse cells" would be clear.

Claim 38 remains indefinite because the phrase "from the 5' and 3' flanking arm of the mouse Rosa26 locus" is unclear and does not clearly set for the structure of the homology arms or that the Rosa26 gene is a mouse Rosa26 gene. 5' and 3' flanking arms are from the Rosa26 gene, not the "position" or "locus" of Rosa26. Replacing "locus" with --gene-- is suggested.

The rejection of claim 39 regarding the term "respectively" has been withdrawn in view of the amendment.

The rejection of claim 40 regarding the term "derived" has been withdrawn in view of the amendment.

Claim 40 as amended is indefinite because it does not clearly set forth the cells are mouse cells. The phrase "wherein the eukaryotic cells are mouse cells" would be clear.

Claim 41 should clearly set forth the vector has the nucleic acid sequence shown in SEQ ID NO: 7.

The rejections of claim 42 have been withdrawn because the claim has been canceled.

Claim 45 remains indefinite because it is unclear what applicants consider an "inactive" positive selection marker. Applicants argue the markers were known to those of skill in the art at the time of filing. Applicants' argument is not persuasive. The phrase was not defined by applicants or those of skill in the art at the time of filing. Therefore, those of skill would not know when they were infringing on the claim.

Claim 46 remains indefinite as amended it appears there are three steps, but only steps a) and b) are specified. Furthermore, it is unclear how the step of "isolating the transgenic non-human mammalian eukaryotic cells" differs from "isolating the transgenic non-human mammalian eukaryotic cells having a modified functional DNA sequence." The phrase "isolating the transgenic non-human mammalian eukaryotic cells having a modified functional DNA sequence" is redundant and should be deleted.

It still cannot be determined how the process of claim 17 further limits the "non-human mammalian eukaryotic cell having a modified Rossa26 locus" as in claim 48. The structure of the cell in claim 48 is not clear from the method of claim 17. Also, a cell

can have a genetically altered Rosa26 gene, but a cell does not have a modified Rosa26 "position" or "locus".

Claims 53-55 remain indefinite as amended because they require providing a eukaryotic cell, a transgenic multi-cell organism or a transgenic non-human mammal using the method of claim 17; however, claim 17 is limited to making a transgenic non-human mammalian eukaryotic cell.

Claims 53-55 are indefinite because "the gene of interest" lacks antecedent basis.

Claims 54 and 55 are indefinite because they do not set forth any steps for "drug development." Evaluating the effect of the drug candidate on a gene of interest does not result in drug development as claimed.

Claim 55 is indefinite because it is unclear how an animal comprising a non-human mammalian cell made by the method of claim 17 is a model of an animal disease.

Claim 56 is indefinite because the metes and bounds of what applicants consider "two mutually incompatible RRSs" does not clearly set forth the structure or function of the acceptor DNA. Clarification is required.

Claim 56 is indefinite because claim 19 does not define a recombination vector. Claim 19 is a method claim.

Claim 56 is indefinite because it cannot be determined how applicants are further limiting the structure of the "functional DNA sequence" in step b).

Claim 56 is indefinite because it does not clearly set forth the recombinase in step c) occurs after step b), which is essential to the invention. Step c) could be performed after step a), which would not work.

Claim Rejections - 35 USC § 102

Claims 17-25, 28-32, 34-38, 43-46, 48 and 53-56 are rejected under 35 U.S.C. 102(b) as being anticipated by Soriano (WO99/53017) for reasons of record.

Soriano made a Rosa26 transgenic mouse by introducing a DNA cassette comprising a LacZ gene flanked by loxP sites into the Rosa26 locus of a mouse ES cell and implanting the ES cell into a mouse blastocyst. The LacZ gene was under the control of the mouse Rosa26 promoter (Example 1, pg 30). Soriano also taught making a Rosa26Cre transgenic mouse (Example 2, pg 41) by introducing a construct into ES cells, the construct comprising a deletor cassette comprising a recombinase gene operably linked to an upstream splice acceptor (SA and a downstream polyA sequence with a positive selection cassette comprising a PGK promoter, the neo gene and a polyadenylation sequence (pg 7, lines 2-10). The construct was inserted into the targeting vector comprising homology arms for the Rosa26 gene and a diphtheria toxin gene for negative selection (pg 7, line 9-10; pg 7, line 1-2). Soriano also made a transgenic mouse by introducing a targeting vector into mouse ES cells, the vector comprising a reporter cassette comprising a splice acceptor operably linked to stuffer DNA flanked by two loxP sites (pg 7, lines 10-16); the stuffer DNA comprised a PGK promoter, the neo gene and four polyA sites (pg 44, Example 3). The methods of Soriano are those claimed.

Applicants argue did not teach introducing an expression cassette comprising a gene of interest operably linked to a promoter. Applicants' argument is not persuasive. Soriano used various fragments of the Rosa26 promoter paragraph bridging pg 34-35. Furthermore, claim 17 encompasses a functional DNA sequence that is i) a gene expression cassette comprising a gene of interest operatively linked to a promoter OR ii) a DNA sequence that can be converted into such a gene expression cassette. LacZ under the control of the endogenous Rosa26 is a DNA sequence that has been converted into a gene expression cassette as claimed.

Applicants argue the converted gene expression cassette must have an exogenous promoter. Applicants' argument is not persuasive because it is unfounded. No such requirement is evident from the specification as originally filed. The claim also encompasses introducing a gene expression cassette having a gene of interest operably linked to a promoter, which is clearly taught in the paragraph on pg 34-35.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

/Michael C. Wilson/
Patent Examiner